

Interleukin-1 Receptor Antagonist-Like Proteins and Uses Thereof," which Applicants contend is clearly indicative of the invention to which the claims are directed.

2. Information Disclosure Statement

The Office Action states that Information Disclosure Statement filed March 26, 1997 fails to comply with the provisions of M.P.E.P. § 609 because an improper form PTO-1449 or equivalent was submitted. Specifically, the Action states that the EMBL database submission listed on the IDS fails to recite the name of the author and the date of publication. The Action also notes that the name of the author and the date of publication for this EMBL database submission has been added to the form PTO-1449, with the corrected document being made of record.

Applicants presume that the Information Disclosure Statement of which the Action refers is the Information Disclosure Statement filed June 21, 2001. Applicants thank the Examiner for correcting the form PTO-1449 by adding the author's name and publication date for the EMBL database submission listed on the IDS. Applicants believe that the corrected form PTO-1449 complies with the provisions of M.P.E.P. § 609, and note that the Action states that the corrected PTO-1449 has been made of record. However, Applicants would be happy to supply an updated copy of the Information Disclosure Statement, and would prefer to have the opportunity if the deficiencies in their previously-submitted Information Disclosure Statement will have the effect of leaving any of the cited references off the front page of any issued patent.

3. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 101

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 101. The Action states that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Applicants traverse this rejection.

Applicants contend that the instant application contains an assertion of a specific and substantial utility for the claimed invention that would be credible to one of ordinary skill in the art. The instant application teaches a nucleotide sequence encoding an amino acid sequence for IL-1ra-L polypeptide (Figures 1A-1B). The instant application also teaches that IL-1ra-L polypeptide shares a high degree of amino acid sequence identity with two other members of the IL-1 family of proteins: IL-1δ (59% identity; 63% similarity) and IL-1ε (44% identity; 63% similarity) (Figure 2). In addition,

the instant application teaches that IL-1ra-L polypeptide shares sequence identity with IL-1 β (31% identity; 45% similarity). With the exception of the amino acid sequence disclosed in GenBank Accession No. BAA84123 (phenol hydroxylase component), which shares the lowest degree of sequence identity with IL-1ra-L polypeptide, *all* of the related amino acid sequences identified in a BLAST search using the IL-1ra-L amino acid sequence (SEQ ID NO: 2) are members of the IL-1 family of proteins (Exhibit A; sequences that were publicly available at the time the instant application was filed are indicated in bold). Based on the expression of human IL-1ra-L mRNA in adult T cells, liver, lung, and spleen; placenta; and fetal kidney, scalp, and eye, as described at page 100, line 31 to page 111, line 4 and page 111, lines 10-11 of the specification, and the teaching that IL-1ra-L polypeptide shares homology with IL-1 δ , IL-1 ϵ , and IL-1 β , one of ordinary skill in the art would recognize that the claimed molecules could be useful, for example, in agonizing an IL-1 receptor in T cells, liver, lung, spleen, kidney, scalp, eye, or placenta.

Exhibit B illustrates that human IL-1ra-L polypeptide shares substantial amino acid sequence identity with a member of the IL-1 family disclosed by Smith *et al.*, 2000, *J. Biol. Chem.* 275:1169-75 (GenBank Accession No. AAF25213, published January 16, 2000; WO 00/71720, published November 30, 2000), and designated as IL-1 η . In addition, Smith *et al.* disclose that the IL-1 η gene possesses a conserved exon-intron structure shared by other members of the IL-1 family and that the IL-1 η gene is located on the long arm of chromosome 2 in a gene cluster with other members of the IL-1 gene family (Smith *et al.*, 2000, *J. Biol. Chem.* 275:1169-75). Applicants also note that because IL-1ra does not induce any intracellular response upon the binding of IL-1 receptor (Arend *et al.*, 1998, *Annu. Rev. Immunol.* 16:27-55), this molecule was designated as a member of the IL-1 family based solely on its amino acid sequence homology to IL-1 β and IL-1 α , similarities in gene structure, and common gene localization to human chromosome 2 (Arend, 1993, *Adv. Immunol.* 54: 167-227). Applicants contend that based on the totality of the evidence of record, one of ordinary skill in the art would recognize that IL-1ra-L polypeptide is a member of the IL-1 family of proteins. In fact, the Smith *et al.* reference cited above indicates that those of ordinary skill in the art, absent Applicants' teaching, *have* recognized that the polypeptide set forth in SEQ ID NO: 2 *is* a member of the IL-1 family of proteins, albeit subsequent to Applicants' identification of this member of the IL-1 family (indeed, after Applicants' priority filing date of December 10, 1999). Moreover, as members

of the IL-1 family have substantial real world use, for example, as agonists or antagonists of inflammatory responses via binding to an interleukin receptor (Gabay, 2000, *Expert Opin. Investig. Drugs* 9:113-27), Applicants contend that one of ordinary skill in the art would recognize that the claimed molecules have credible, specific, and substantial utility.

Applicants contend that because the instant application contains an assertion of a specific and substantial utility for the claimed invention credible to one of ordinary skill in the art, the rejection under 35 U.S.C. § 101 should be withdrawn.

4. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that since the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention.

Applicants have set forth affirmative evidence that the asserted utility would be credible to one of ordinary skill in the art. Applicants contend that because the instant application contains an assertion of a specific and substantial utility for the claimed invention that one of ordinary skill in the art would find to be credible, this rejection should be withdrawn.

The Office Action also asserts a rejection of claims 1, 2, 4-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that a deposit of biological material is necessary for the enablement of the claims because the specification does not provide a repeatable method for obtaining ATCC Deposit No. PTA-1215 and this deposit does not appear to be a readily available material. The Action also states that a deposit made in full compliance with 37 C.F.R. §§ 1.803-1.809 would satisfy the requirements of 35 U.S.C. § 112, first paragraph, provided that Applicants submit an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that a deposit has been made under the terms of the Budapest Treaty and that

all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

Pursuant to the Examiner's request, Applicants submit herewith a Declaration stating that a deposit complying with 37 C.F.R. §§ 1.801-1.809 was made under the provisions of the Budapest Treaty. Applicants contend that all the requirements of 37 C.F.R. §§ 1.801-1.809 have been met. *In re Lundak*, 225 U.S.P.Q. 90 (Fed. Cir. 1985). Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 2-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the genus of IL-1ra-L variants recited in claims 2 and 3 is highly variant, and the specification fails to describe the common attributes or characteristics identifying the members of this genus, or provide a representative number of species to describe this genus, the Applicants were not in possession of the claimed genus of nucleic acid molecules at the time the application was filed.

Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, encoding a polypeptide fragment of at least 25 amino acid residues; a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, comprising a fragment of at least 16 nucleotides; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of either of these nucleic acid molecules; or a nucleotide sequence complementary to the nucleotide sequence of any of the above nucleic acid molecules. Applicants contend that because claim 2, as amended, recites only fragments of the disclosed human IL-1ra-L nucleic acid molecule (*i.e.*, SEQ ID NO: 1), one of ordinary skill in the art could readily determine the structure of nucleic acid molecules falling within the scope of this claim. Applicants therefore respectfully request that this ground of rejection be withdrawn.

Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2; a nucleotide sequence encoding a polypeptide as set

forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 25 amino acid residues; a region of the nucleotide sequence of any of these nucleic acid molecules comprising a fragment of at least 16 nucleotides; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of the above nucleic acid molecules; or a nucleotide sequence complementary to any of the above nucleic acid molecules. Applicants note that the instant application teaches the amino acid sequence for human IL-1ra-L polypeptide (Figures 1A-1B) and an amino acid sequence alignment (Figure 2) demonstrating that IL-1ra-L polypeptide shares a high degree of amino acid sequence identity with two other members of the IL-1 family of proteins: IL-1 δ (59%) and IL-1 ϵ (44%). The instant application also teaches that regions in IL-1ra-L polypeptide that are tolerable to conservative amino acid substitution can be identified by performing sequence comparisons between IL-1ra-L polypeptide and other related polypeptides (page 21, line 31 to page 22, line 13). The instant application further sets forth in Table I (page 21) rubrics recognized in the art for making conservative amino acid substitutions. In view of the teachings in the instant application, Applicants respectfully contend that one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Thus, Applicants respectfully contend that their specification fulfills the requirements of 35 U.S.C. § 112, first paragraph, and request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 2-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for a nucleic acid encoding a polypeptide as set forth in SEQ ID NO: 2, does not reasonably provide enablement for a nucleic acid encoding a polypeptide which is "at least about 70% identical to the polypeptide of SEQ ID NO: 2" or a nucleic acid molecule encoding a substitution, insertion, or deletion mutant of the polypeptide of SEQ ID NO: 2. The Action states that because the claims are overly broad, no guidance is provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid molecule encoding an IL-1ra-L polypeptide other than the one exemplified in the specification, and it is known in the art that even a single amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

As described above, Applicants have amended claims 2 and 3 so that they no longer recite

nucleic acid molecules comprising either a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2; a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion; or a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion. Applicants contend that the claims, as amended, are not overly broad, and that in view of the specification's teachings, one of ordinary skill in the art could readily make and use the claimed nucleic acid molecules. Moreover, Applicants contend that while the references cited in the Action may teach that an amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, these references do *not* teach that a *conservative* amino acid substitution would have this effect. Specifically, Mikayama *et al.*, 1993, *Proc. Natl. Acad. Sci. U.S.A.* 90:10056-60, teach that an asparagine-to-serine substitution at position 106 in human GIF destroys GIF function, and Voet *et al.*, *Biochemistry* 126-28, 228-34 (1990), teach that a glutamic acid-to-valine substitution in beta hemoglobin results in sickle-cell anemia. These are *not* "conservative substitutions" as that term is understood by those with skill in the art *or* as explicitly defined in the instant specification. Applicants note that the instant specification does not teach that an asparagine-to-serine substitution or a glutamic acid-to-valine substitution is either exemplary or preferred (Table I; page 22). Applicants contend that, in view of the specification's explicit teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to make and use the claimed invention, and therefore, Applicants respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

5. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

The Action first asserts that claims 1-3 are indefinite for reciting the phrase "hybridizes under

moderately or highly stringent conditions” because this phrase is relative and conditional. The Action states that some nucleic acids that might hybridize under conditions of moderate stringency would fail to hybridize under conditions of high stringency. Applicants note that the specification defines the meaning of the terms “moderately stringent conditions” (page 17, lines 12-18) and “highly stringent conditions” (page 16, lines 6-13), and provides examples of each. However, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention, Applicants have amended claims 1-3 to recite that the claimed nucleic acid molecules comprise a nucleotide sequence that “hybridizes under at least moderately stringent conditions.” Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 2 is vague for reciting the phrase “about 70% identical” because the term “about” is inherently vague and indefinite. As discussed in section 3 above, Applicants have amended claim 2 so that it no longer recites a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2. In addition, Applicants have amended claim 2 to replace the term “at least about 25 amino acid residues” with the term “at least 25 amino acid residues,” and claims 2 and 3 to replace the term “at least about 16 nucleotides” with the term “at least 16 nucleotides.” Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 2 and 3 are vague and indefinite for reciting the phrase “has an activity of the polypeptide set forth in...SEQ ID NO: 2” because the activity of the polypeptide encoded by the nucleic acid being claimed is unclear. While Applicants respectfully disagree with the assertion that this phrase is indefinite, in an effort to expedite the present application to allowance Applicants have amended the pending claims to delete the phrase objected to in the Action, and affirmatively recite that C- and/or N- terminally truncated IL-1ra-L polypeptide variants must comprise at least 25 amino acid residues. Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 10 is vague and indefinite for reciting the phrase “other than the promoter DNA for the native IL-1ra-L polypeptide” because it is unclear which promoter DNA is being excluded and which is being included in the claim. Applicants have amended claim 10

to recite that "the nucleic acid molecule comprises promoter DNA other than native IL-1ra-L promoter DNA." Applicants contend that because it is clear which promoter DNA is being excluded and which is being included, claim 10 is not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 46 is indefinite for reciting the term "fragment[s] thereof" because this term encompasses potentially any portion of the heterologous polypeptide including a single amino acid. Applicants have amended claim 46 to recite that the IgG constant domain fragment must be "biologically-active," and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 45 and 46, which are dependent upon non-elected claims 13, 14, or 15, should be amended to be dependent upon on elected nucleic acid claims, since the nucleic acid is utilized in production of the fusion proteins. Applicants have amended claims 45 and 46 to recite a nucleic acid molecule encoding a fusion polypeptide comprising the nucleic acid molecule of any of claims 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence. Because claims 45 and 46, as amended, are no longer dependent upon non-elected claims 13, 14, or 15, Applicants request that this ground of rejection be withdrawn.

The Action next asserts that claims 4-8, 11, and 42-44 are vague and indefinite for being dependent upon claims 1 and 2 for their limitations. Applicants contend that the claims, as amended, satisfy the requirements of 35 U.S.C. § 112, second paragraph, and therefore, respectfully contend that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

6. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(a), as being anticipated by International Publication No. WO 99/37662 (published July 29, 1999), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding a SPOIL protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit

to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in International Publication No. WO 99/37662 shares a sequence identity of 7.5% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit C). In view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 17, lines 17-18), it is quite apparent that the cDNA molecule disclosed in WO 99/37662 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 4 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent identical* to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in WO 99/37662. Applicants contend, therefore, that International Publication No. WO 99/37662 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(b), as being anticipated by European Patent Application No. EP 0 855 404 (published July 29, 1998), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an IL-1ra beta protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in European Patent Application No. EP 0 855 404 shares a sequence identity of 44.3% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit D). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in EP 0 855 404 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 4 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in

SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent identical* to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in EP 0 855 404. Applicants contend, therefore, that European Patent Application No. EP 0 855 404 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, and 42, under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent No. 5,075,222 (issued December 24, 1991), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an IL-1ra protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in U.S. Patent No. 5,075,222 shares a sequence identity of 24.4% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit E). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in U.S. 5,075,222 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 4 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent identical* to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in U.S. 5,075,222. Applicants contend, therefore, that U.S. Patent No. 5,075,222 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

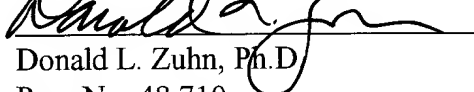
CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Mertz believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: January 16, 2003

By: 
Donald L. Zuhn, Ph.D.
Reg. No. 48,710

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-1214)

PATENT

In re Application of: Welcher et al.)

Serial No.: 09/723,676)

Filed: November 28, 2000)

For: Interleukin-1 Receptor)
Antagonist-Like Molecules)
and Uses Thereof)

Before the Examiner: P. Mertz

Group Art Unit: 1646

Commissioner for Patents
Washington, D.C. 20231

Sir:

TECH CENTER 1600/2900

JAN 22 2003

RECEIVED

DECLARATION

1. Applicants deposited cDNA encoding human IL-1ra-L polypeptide with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209.

2. The deposit was accepted by the ATCC, an International Depository Authority, under the provisions of the Budapest Treaty, and the deposit was designated as PTA-1215. A copy of the ATCC receipt for this deposit, showing the patent deposit designation (Accession No. PTA-1215) and the date on which the deposit was received by the ATCC (January 20, 2000) is attached.

3. Pursuant to 37 C.F.R. § 1.808(a)(2), the deposit was made under conditions that assure that all restrictions imposed by the depositors on the availability to the public of the deposited material would be irrevocably removed upon the granting of a patent relying on the deposited biological material.

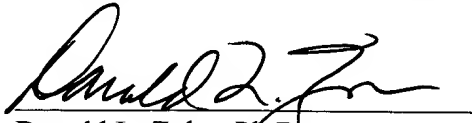
4. In making the deposit, Applicants acknowledged their responsibility, pursuant to 37 C.F.R. § 1.805, to provide a replacement or supplemental deposit if the depository possessing the deposit is unable to furnish samples thereof or is able to furnish samples thereof but the deposit has become contaminated or has lost its capability to function as described in the specification.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: January 16, 2003

By:


Donald L. Zuhn, Ph.D.
Reg. No. 48,710

ATCC

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-365-2745

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Amgen Inc.
Attn: Dawn Pohl
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Deposited on Behalf of: Amgen Inc. (Ref. A-637-P)

Identification Reference by Depositor:

Patent Deposit Designation

Human IL-1ra like cDNA subcloned into the pGME-T easy
Vector and transfected into DH10B bacteria

PTA-1215

The deposit was accompanied by: ☐ a scientific description ☒ a proposed taxonomic description indicated above.

The deposit was received January 20, 2000 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: ☒ We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested February 1, 2000. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Barbara M. Hailey
Barbara M. Hailey, Administrator, Patent Depository

Date: February 1, 2000

cc: Scott N. Bernstein

EXHIBIT A

BLASTP 2.2.5 [Nov-16-2002]

Reference:

Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1041959765-016166-6258

Query=

(157 letters)

Database: All non-redundant GenBank CDS

translations+PDB+SwissProt+PIR+PRF

1,292,592 sequences; 412,925,052 total letters

Related Structures

Sequences producing significant alignments:	Score (bits)	E Value
gi 6694394 gb AAF25213.1 AF201833_1 FIL1 eta [Homo sapiens]	323	5e-88
gi 20822718 ref XP_130058.1 RIKEN cDNA 2310043N20 [Mus mus...	208	2e-53
gi 25008591 sp Q9D6Z6 IIF8_MOUSE Interleukin 1 family membe...	206	6e-53
gi 20070252 ref NP_055253.2 interleukin 1 family, member 8...	187	4e-47
gi 9665234 ref NP_062564.1 interleukin 1 family, member 9;...	139	1e-32
gi 7657092 ref NP_055255.1 interleukin 1 family, member 6 ...	139	1e-32
gi 20822740 ref XP_130067.1 IL-1F9 [Mus musculus] >gi 2394...	137	4e-32
gi 9506601 ref NP_062323.1 interleukin 1 family, member 9;...	116	9e-26
gi 19068184 gb AAL67151.1 IL-1F7d [Homo sapiens]	89	2e-17
gi 10185738 gb AAG14421.1 AF251119_1 interleukin-1-related ...	89	3e-17
gi 6694392 gb AAF25212.1 AF201832_1 FIL1 zeta [Homo sapiens]	89	3e-17
gi 20127524 ref NP_055254.2 interleukin 1 family, member 7...	89	3e-17
gi 25008597 sp Q9QYY1 IIF5_MOUSE Interleukin 1 family membe...	79	2e-14
gi 9506807 ref NP_062324.1 interleukin 1 family, member 5 ...	79	2e-14
gi 6912432 ref NP_036407.1 interleukin 1 family, member 5 ...	78	4e-14
gi 23346487 ref NP_694717.1 IL-1F10 [Mus musculus] >gi 250...	75	3e-13
gi 25008589 sp Q8WWZ1 IIFA_HUMAN Interleukin 1 family membe...	74	5e-13
gi 20127669 ref NP_115945.3 putative interleukin-1 recept...	74	6e-13
gi 124313 sp P25085 IL1X_MOUSE Interleukin-1 receptor antag...	74	7e-13
gi 19068186 gb AAL67154.1 IL-1F7e [Homo sapiens]	74	9e-13
gi 238585 gb AAB20265.1 interleukin 1 receptor antagonist ...	73	1e-12
gi 13624317 ref NP_112444.1 interleukin 1 receptor antagon...	73	1e-12
gi 10185740 gb AAG14422.1 interleukin-1-related protein sh...	73	1e-12
gi 198390 gb AAA39310.1 interleukin 1 receptor antagonist	73	1e-12
gi 12829966 gb AAK01948.1 interleukin-1 receptor antagonis...	73	2e-12
gi 11559964 ref NP_071530.1 interleukin 1 receptor antagon...	72	4e-12
gi 6166230 sp O18999 IL1X_HORSE INTERLEUKIN-1 RECEPTOR ANTA...	68	4e-11
gi 3211711 gb AAC39257.1 interleukin-1 receptor antagonist...	68	5e-11
gi 1274 emb CAA38566.1 interleukin-1 beta [Ovis aries]	68	5e-11
gi 12746561 gb AAK01472.1 interleukin-1 receptor antagonis...	68	5e-11
gi 124312 sp P18510 IL1X_HUMAN Interleukin-1 receptor antag...	68	5e-11
gi 2997621 gb AAC39672.1 interleukin-1 intracellular recep...	67	6e-11
gi 999512 pdb 1IRP Interleukin-1 Receptor Antagonist Prot...	67	6e-11
gi 6016361 sp Q29056 IL1X_PIG INTERLEUKIN-1 RECEPTOR ANTAGO...	67	6e-11
gi 69700 pir ICB01B interleukin-1 beta precursor - bovine ...	67	6e-11
gi 124314 sp P26890 IL1X_RABIT INTERLEUKIN-1 RECEPTOR ANTAG...	67	8e-11
gi 7438656 pir A39386 interleukin-1 receptor antagonist, l...	67	8e-11
gi 10835147 ref NP_000568.1 interleukin 1 receptor antagon...	67	9e-11

gi 6016360 sp O77482 IL1X_BOVIN INTERLEUKIN-1 RECEPTOR ANTA...	67	1e-10
gi 996127 pdb 1ILR 2 Chain 2, Interleukin 1 Receptor Antago...	67	1e-10
gi 124307 sp P21621 IL1B_SHEEP INTERLEUKIN-1 BETA PRECURSOR...	66	1e-10
gi 124302 sp P09428 IL1B_BOVIN INTERLEUKIN-1 BETA PRECURSOR...	65	3e-10
gi 9836542 dbj BAB11806.1 interleukin-1 receptor antagonis...	65	3e-10
gi 3211709 gb AAC39256.1 interleukin-1 beta [Equus caballus]	65	4e-10
gi 6166229 sp Q28386 IL1B_HORSE Interleukin-1 beta precurs...	64	6e-10
gi 11526781 gb AAG36777.1 AF216526_1 interleukin-1 receptor...	64	8e-10
gi 7438655 pir JC5646 interleukin-1 beta - horse >gi 24635...	63	1e-09
gi 124305 sp P26889 IL1B_PIG INTERLEUKIN-1 BETA PRECURSOR (...)	63	1e-09
gi 481234 pir S38373 interleukin-1 beta precursor - pig >g...	63	1e-09
gi 17367201 sp Q9WVG1 IL1B_CAVPO Interleukin-1 beta precurs...	63	2e-09
gi 1708445 sp P51745 IL1B_CEREL Interleukin-1 beta precurs...	62	2e-09
gi 15489057 gb AAH13644.1 Similar to replication initiatio...	62	2e-09
gi 6016358 sp P79162 IL1B_CAPHI INTERLEUKIN-1 BETA PRECURSO...	62	2e-09
gi 3024024 sp P79182 IL1B_MACFA INTERLEUKIN-1 BETA PRECURSO...	61	5e-09
gi 1352451 sp P48090 IL1B_MACMU INTERLEUKIN-1 BETA PRECURSO...	61	5e-09
gi 1708446 sp P51493 IL1B_MACNE INTERLEUKIN-1 BETA PRECURSO...	61	5e-09
gi 186288 gb AAA59136.1 interleukin 1	61	6e-09
gi 18033002 gb AAL56945.1 AF320322_1 interleukin-1 precurs...	61	6e-09
gi 15213526 gb AAK92041.1 AF294754_1 interleukin-1 beta [Sa...	60	7e-09
gi 6680415 ref NP_032387.1 interleukin 1 beta [Mus musculu...	60	7e-09
gi 26225025 gb AAN76442.1 interleukin-1 beta precursor [Ma...	60	1e-08
gi 124306 sp P14628 IL1B_RABIT INTERLEUKIN-1 BETA PRECURSOR...	60	1e-08
gi 494810 pdb 2MIB Interleukin-1 Beta (IL-1 Beta) >gi 231...	60	1e-08
gi 1170531 sp P41687 IL1B_FELCA INTERLEUKIN-1 BETA PRECURSO...	60	1e-08
gi 10835145 ref NP_000567.1 interleukin 1, beta [Homo sapi...	59	2e-08
gi 124303 sp P01584 IL1B_HUMAN Interleukin-1 beta precursor...	59	2e-08
gi 6520194 dbj BAA87947.1 interleukin-1 beta [Tursiops tru...	59	2e-08
gi 208635 gb AAA72561.1 interleukin 1-beta	59	3e-08
gi 494152 pdb 1HIB Interleukin-1 Beta (Human) Mutant With...	58	4e-08
gi 26225027 gb AAN76443.1 interleukin-1 beta precursor [Pa...	58	4e-08
gi 2905622 gb AAC03536.1 interleukin 1 beta [Homo sapiens]	58	4e-08
gi 1827779 pdb 1IOB Interleukin-1 Beta From Joint X-Ray A...	58	5e-08
gi 208637 gb AAA72849.1 growth hormone:interleukin 1-beta ...	58	5e-08
gi 230947 pdb 41BI Interleukin-1Beta (IL-1Beta) (Mutant W...	58	5e-08
gi 17367239 sp Q9XS77 IL1B_TRIVU Interleukin-1 beta precurs...	58	5e-08
gi 1170530 sp P46648 IL1B_CERTO INTERLEUKIN-1 BETA PRECURSO...	57	6e-08
gi 16417601 gb AAL18817.1 AF421387_1 interleukin 1 beta pre...	57	1e-07
gi 13928692 ref NP_113700.1 interleukin 1 beta [Rattus nor...	56	2e-07
gi 3175996 emb CAA75239.1 interleukin-1beta [Gallus gallus...	55	3e-07
gi 230410 pdb 21BI Interleukin-1Beta (IL-1Beta) (Mutant W...	54	6e-07
gi 230798 pdb 31BI Interleukin-1Beta (IL-1Beta) (Mutant W...	54	7e-07
gi 5777787 emb CAB53499.1 interleukin-1-beta [Xenopus laevis]	49	2e-05
gi 6468654 emb CAB53541.3 interleukin-1 beta 2 precursor [...]	48	5e-05
gi 25956174 emb CAC33867.2 interleukin 1 beta protein [Sco...	48	5e-05
gi 3805826 emb CAA06157.1 interleukin-1 beta [Oncorhynchus...	47	7e-05
gi 18152761 emb CAC83518.1 interleukin-1 beta [Oncorhynchu...	47	8e-05
gi 2821975 dbj BAA24538.1 interleukin-1 beta [Cyprinus car...	47	1e-04
gi 5708097 emb CAB52366.1 interleukin-1-beta [Cyprinus car...	47	1e-04
gi 19911215 dbj BAB86882.1 IL-1b [Paralichthys olivaceus]	45	4e-04
gi 3687837 gb AAC62237.1 interleukin-1 receptor antagonist...	45	5e-04
gi 25137090 emb CAD12102.1 interleukin-1 beta-1 [Carassius...	42	0.002
gi 12049719 emb CAC19888.1 interleukin 1 beta 2-2 [Cyprinu...	41	0.005
gi 12049717 emb CAC19887.1 interleukin 1 beta 2-1 [Cyprinu...	40	0.009
gi 14330417 emb CAC41006.1 Interleukin-1 beta [Dicentrarch...	39	0.025
gi 25137092 emb CAD12103.1 interleukin-1 beta-2 [Carassius...	36	0.20
gi 16945693 emb CAD11603.1 interleukin-1 beta [Sparus aura...	33	1.1
gi 6016355 sp P79161 IL1A_CAPHI INTERLEUKIN-1 ALPHA PRECURS...	33	1.2
gi 539767 pir A61246 interleukin-1 alpha precursor - sheep	32	2.3
gi 3687909 gb AAD04132.1 interleukin-1 receptor antagonist...	32	3.6
gi 5851794 dbj BAA84123.1 phenol hydroxylase component [Ra...	31	4.5

EXHIBIT B

Aligned Length = 157 Gaps = 0
Identities = 157 (100%) Similarities = 0 (0%)

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IL-1ra-L      1 MNPQREAAPKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRD  50
AAF25213      1 MNPQREAAPKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRD  50
                *****

IL-1ra-L      51 TEFSDKEKGNMVYLGIGKDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKA 100
AAF25213      51 TEFSDKEKGNMVYLGIGKDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKA 100
                *****

IL-1ra-L     101 QKPFLFFHNKEGSTSVFQSVSYPGWFIATSTTSGQPIFLTKERGITNNTN 150
AAF25213     101 QKPFLFFHNKEGSTSVFQSVSYPGWFIATSTTSGQPIFLTKERGITNNTN 150
                *****

IL-1ra-L     151 FYLDSVE 157
AAF25213     151 FYLDSVE 157
                *****
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EXHIBIT C

	10	20	30	40	50
IL-1ra-L	GTGTTGCTCCACTGTCAGTCCTCCAGAGCCTCAAGAGATCTTTGGGCCAT CACAACGAGGTGACAGTCAGGAGGTCTCGGAGTTCTCTAGAAACCCGGTA				
1. SPOIL I	500 510				
[130]	AAGACACCCCT-AACAAA> 				
IL-1ra-L	AAGAGATCTTTGGGCCAT				
	60	70	80	90	100
IL-1ra-L	ATCAGCTTCTTTCCAAAATGAACACACCCAGGGGCAGGAAAGAATGCTC TAGTCGAAAGAAAGGTTTACTTGTGTGGGTCCCCGTCCTTTCTTACGAG				
1. SPOIL I	520	530	540	550	
[130]	AT-GGAAGAC--T-GAAAA-GAA-A-GCTGA-GCCCTCCCTGGGCTG-TT> 				
IL-1ra-L	ATCAGCTTCTTTCCAAAATGAACACACCCAGGGGCAGGAAAGAATGCTC				
	110	120	130	140	150
IL-1ra-L	TTTCCTTGGTCATTAAGGGGCCTGGGAGTCCTGGACCAGCTTTTCATGCA AAAGGAACCAGTAATTCCCCGGACCCTCAGGACCTGGTCGAAAAGTACGT				
					AA
1. SPOIL I	560	570	580	590	600
[130]	TTTCCTTGGTGGTGAATCAGATGAAGAACATCTTACCATGTTTTCATCCA> 				
IL-1ra-L	TTTCCTTGGTGAATTAAGGGGCCTGGGAGTCCTGGACCAGCTTTTCATGCA				
	160	170	180	190	200
IL-1ra-L	GCTAGACCACTTACATGCAACTAGAGCCTTGACTTTGAAACGAGGGACAA CGATCTGGTGAATGTACGTTGATCTCGGAAGTGAAGTCTTGGTCCCTGTT				
1. SPOIL I	610	620	630	640	650
[130]	GCATTTACTGTTGGTTTTTAC-A-AGGAGTGAATTTTTTA--A--AATAA> 				
IL-1ra-L	GCTAGACCACTTACATGCAACTAGAGCCTTGACTTTGAAACGAGGGACAA				
	210	220	230	240	250
IL-1ra-L	AAGCATCTCTTGCTAAAGGTAACCTCTGCTGCTTAGAACCCAGCCTCCTC TTCGTAGAGAACGATTTCCATTGAAGACGACGAATCTGGGTCTGGAGGAG				
1. SPOIL I	660	670			
[130]	AATCATTTATCTCATAAAAAA> 				
IL-1ra-L	AAGCATCTCTTGCTAAAGGTAA				

IL-1ra-L	260	270	280	290	300
	ACCACCATCTGATCTATCTTGTTCCTTCACAAAAGGCTCTGAAGACATC				
	TGGTGGTAGACTAGATAGAACAAGAGAAGTGTTCCTCGAGACTTCTGTAG				
IL-1ra-L	310	320	330	340	350
	ATGAACCCACAACGGGAGGCAGCACCCAAATCCTATGCTATTCGTGATTC				
	TACTTGGGTGTTGCCCTCCGTCGTGGGTTTAGGATACGATAAGCACTAAG				
IL-1ra-L	360	370	380	390	400
	TCGACAGATGGTGTGGGTCCTGAGTGGAAATTCTTTAATAGCAGCTCCTC				
	AGCTGTCTACCACACCCAGGACTCACCTTTAAGAAATTATCGTCGAGGAG				
IL-1ra-L	410	420	430	440	450
	TTAGCCGCAGCATTAAGCCTGTCACTCTTCATTTAATAGCCTGTAGAGAC				
	AATCGGCGTCGTAATTCGGACAGTGAGAAGTAAATTATCGGACATCTCTG				
IL-1ra-L	460	470	480	490	500
	ACAGAATTCAGTGACAAGGAAAAGGTAATATGGTTTACCTGGGAATCAA				
	TGTCTTAAGTCACTGTTCTTTTCCATTATACCAAATGGACCCTTAGTT				
IL-1ra-L	510	520	530	540	550
	GGGAAAAGATCTCTGTCTTCTGTGCAGAAATTCAGGGCAAGCCTACTT				
	CCCTTTTCTAGAGACAGAGAAGACACGTCTTTAAGTCCCGTTCGGATGAA				
IL-1ra-L	560	570	580	590	600
	TGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCA				
	ACGTCGAATTCCTTTTTTTATAGTACCTGGACATACACCTCTTCTTTCGT				
IL-1ra-L	610	620	630	640	650
	CAGAAGCCCTTTCTCTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTT				
	GTCTTCGGGAAAGAGAAAAAGGTGTTATTTCTTCCGAGGTGAAGACAGAA				
IL-1ra-L	660	670	680	690	700
	TCAGTCAGTCTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAG				
	AGTCAGTCAGAGAATGGGACCGACCAAGTATCGGTGGAGGTGGTGTAGTC				
IL-1ra-L	710	720	730	740	750
	GACAGCCCATCTTTCTCACCAGGAGAGAGGCATAACTAATAACACTAAC				
	CTGTCGGGTAGAAAGAGTGGTTCCTCTCTCCGTATTGATTATTGTGATTG				
IL-1ra-L	760	770	780	790	800
	TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG				
	AAGATGAATCTAAGACACCTATTTAGGTCGGATCCGACACCCACCGACC				

IL-1ra-L	810	820	830	840	850
	TTCCAGGATAGAGAATCAAGCTGTCAGAGTCATCTTAACAGATCATTATG				
	AAGGTCCTATCTCTTAGTTCGACAGTCTCAGTAGAATTGTCTAGTAATAC				
IL-1ra-L	860	870	880	890	900
	CGACTGAGTTCACCTAGCAGTTCAGCCCATCCATAGCTTACCTCATTCTTA				
	GCTGACTCAAGTGATCGTCAAGTCGGGTAGGTATCGAATGGAGTAAGAAT				
IL-1ra-L	910	920	930	940	950
	CTATCCAAAAGCCACCTCCTCCTCCAAACATCCATTTCTGTACCAAGACC				
	GATAGGTTTTTCGGTGGAGGAGGAGGTTTGTAGGTAAAGACATGGTTCTGG				
IL-1ra-L	960	970	980	990	1000
	CTCACTCGAATGTCCTATCCCAAGATGAAACCTAAAAATCACTTTCCAT				
	GAGTGAGCTTACAGTGATAGGGTCTACTTTGGATTTTTAGTGAAAGGTA				
IL-1ra-L	1010	1020	1030	1040	1050
	TCTTTCTTGATCTTACCCACCATCCACTCAGCTGCCATGCCAGTTTAG				
	AGAAAGAACTAGAATGGGGTGGTAGGTGAGTCGACGGTACGGGTCAAATC				
IL-1ra-L	1060	1070	1080	1090	1100
	TTAACCCCCCAAATGCTGCTTCATGCAACCTTCCATTCCCTATTCCTTTTG				
	AATTGGGGGGTTTACGACGAAGTACGTTGGAAGGTAAGGATAAGGAAAAAC				
IL-1ra-L	1110	1120	1130	1140	1150
	CCAACCCATGATGTAGAGATGTGGATTCATGACATTTTGTTCATACAAC				
	GGTTGGGTACTACATCTCTACACCTAAGTACTGTAAACAAGTATGTTGA				
IL-1ra-L	1160	1170	1180	1190	1200
	TCTTCAATAAAACATTATAATATGTGCCCCAAAGATAAAGCTGAAGAATG				
	AGAAGTTATTTTGTAATATTATACACGGGGTTTCTATTTGACTTCTTAC				
IL-1ra-L	1210	1220	1230	1240	
	AGATGAATGTGAAATTAAAGGTTTGCATGTCTTCCTAATCCTAA				
	TCTACTTACACTTTAATTTCCAAACGTACAGAAGGATTAGGATT				

EXHIBIT D

	10	20	30	40	50
IL-1ra-L	GTGTTGCTCCACTGTCAGTCCCTCCAGAGCCTCAAGAGATCTTTGGGCCAT CACAACGAGGTGACAGTCAGGAGGTCTCGGAGTTCTCTAGAAACCCGGTA				
	60	70	80	90	100
IL-1ra-L	ATCAGCTTTCTTTCCAAAATGAACACACCCAGGGGCAGGAAAGAATGCTC TAGTCGAAAGAAAGGTTTACTTGTGTGGGTCCCCGTCTTTCTTACGAG				
	110	120	130	140	150
IL-1ra-L	TTTCCTTGGTCATTAAGGGCCTGGGAGTCCTGGACCAGCTTTTCATGCA AAAGGAACCACTAATTCCCCGGACCCCTCAGGACCTGGTCGAAAAGTACGT				
	160	170	180	190	200
IL-1ra-L	GCTAGACCACTTACATGCAACTAGAGCCTTGACTTTGAAACGAGGGACAA CGATCTGGTGAATGTACGTTGATCTCGGAACTGAAACTTTGCTCCCTGTT				
1. IL-1ra β [882]				10	
				ACGAGCCACGA>	
IL-1ra-L				ACGAGGGACAA	
	210	220	230	240	250
IL-1ra-L	AAGCATCTCTTGCTAAAGGTAACCTCTGCTGCTTAGAACCCAGCCTCCTC TTCGTAGAGAACGATTTCCATTGAAGACGACGAATCTTGGGTCGGAGGAG				
1. IL-1ra β [882]	20	30	40	50	60
	TTCAGTCCCCTG--GACTGTAGATAAAGACCCTTTCTTGCCAG-GTGCTG>				
IL-1ra-L	AAGCATCTCTTGCTAAAGGTAACCTCTGCTGCTTAGAACCCAGCCTCCTC				
	260	270	280	290	300
IL-1ra-L	ACCACCATCTGATCTATCTTGTCTCTTCACAAAAGGCTCTGAAGACATC TGGTGGTAGACTAGATAGAACAAGAGAAGTGTTTCCGAGACTTCTGTAG				
				G	
1. IL-1ra β [882]	70	80	90	100	110
	A-GACAACCACA-CTATGAGAGGCACTCCAGGAGACGCTATGGTGGAGGA>				
IL-1ra-L	ACCACCATCTGATCTATCTTGTCTCTTCACAAAAGGCTCTGAAGACATC				
	310	320	330	340	350
IL-1ra-L	ATGAACCCACAACGGGAGGCAGCACCCAAATCCTATGCTATTCGTGATTCT TACTTGGGTGTTGCCCTCCGTCGTGGGTTTAGGATACGATAAGCACTAAG				

		GT			A
1. IL-1ra β	120	130	140		160
[882]	AGGGCCCTATCAATCAATGTGTAAACCTATTACTGGGCTATTAATGATTT>				
IL-1ra-L	ATGAACCCACAACGGGAGGCAGCACCCAAATCCTATGCTATTTCGTGATTC				
	360	370	380	390	400
IL-1ra-L	TCGACAGATGGTGTGGGTCCTGAGTGGAAATTCTTTAATAGCAGCTCCTC				
	AGCTGTCTACCACACCCAGGACTCACCTTTAAGAAATTATCGTCGAGGAG				
			T		
1. IL-1ra β	170	180	190	200	210
[882]	GAATCAGCAAGTGTGGACCCCTCAGGGTCAGAACCTT-GTGGCAGTTCCAC>				
IL-1ra-L	TCGACAGATGGTGTGGGTCCTGAGTGGAAATTCTTTAATAGCAGCTCCTC				
	410	420	430	440	450
IL-1ra-L	TTAGCCGCAGCATTAAGCCTGTCACTCTTCATTTAATAGCCTGTAGAGAC				
	AATCGGCGTCGTAATTCGGACAGTGAGAAGTAAATTATCGGACATCTCTG				
1. IL-1ra β	220	230	240	250	260
[882]	GAAGTGACAGTGTGACCCCACTGTTGCTGTTATCACATGCAAGTAT>				
IL-1ra-L	TTAGCCGCAGCATTAAGCCTGTCACTCTTCATTTAATAGCCTGTAGAGAC				
	460	470	480	490	500
IL-1ra-L	ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTACCTGGGAATCAA				
	TGTCTTAAGTCACTGTTCTTTTCCATTATACCAAATGGACCCTTAGTT				
		G			
1. IL-1ra β	270	280	290	300	310
[882]	CCAGAGGCTCTTGACAAGGCAGAGGG-GATCCCATTTATTTGGGAATCCA>				
IL-1ra-L	ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTACCTGGGAATCAA				
	510	520	530	540	550
IL-1ra-L	GGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCCTACTT				
	CCCTTTTCTAGAGACAGAGAAGACACGTCTTTAAGTCCCGTTCGGATGAA				
				C	
1. IL-1ra β	320	330	340	350	360
[882]	GAATCCAGAAATGTGTTTGTATTGTG-AGAAGGTTGAGAAAGCCACAT>				
IL-1ra-L	GGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCCTACTT				

	560	570	580	590	600
IL-1ra-L	TGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCA ACGTCGAATTCCTTTTTTTATAGTACCTGGACATACACCTCTTCTTTCGT				
1. IL-1ra β	370	380	390	400	410
[882]	TGCAGCTAAAAGAGCAGAAGATCATGGATCTGTATG-GCCAACCCGAGCC> 				
IL-1ra-L	TGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCA				
	610	620	630	640	650
IL-1ra-L	CAGAAGCCCTTTCTCTTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTT GTCTTCGGGAAAGAGAAAAAGGTGTTATTTCTTCGAGGTGAAGACAGAA				
	G				
1. IL-1ra β	420	430	440	450	460
[882]	CTGAAACCCTTCTTTTCTACCGTGCCAAGACTGGTAGGACCTCCACCCT> 				
IL-1ra-L	CAGAAGCCCTTTCTCTTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTT				
	660	670	680	690	700
IL-1ra-L	TCAGTCAGTCTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAG AGTCAGTCAGAGAATGGGACCGACCAAGTATCGGTGGAGGTGGTGTAGTC				
1. IL-1ra β	470	480	490	500	510
[882]	TGAGTCTGTGGCCTTCCCGGACTGGTTCATTGCCTCCTCCA--AGA-GAG> 				
IL-1ra-L	TCAGTCAGTCTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAG				
	710	720	730	740	750
IL-1ra-L	GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC CTGTCGGGTAGAAAGAGTGGTTCCTCTCTCCGTATTGATTATTGTGATTG				
1. IL-1ra β	520	530	540	550	560
[882]	ACCAGCCCATCATTCTGACTTCAGAACTTGGGAAGTCATACAACACTGCC> 				
IL-1ra-L	GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC				
	760	770	780	790	800
IL-1ra-L	TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG AAGATGAATCTAAGACACCTTATTTAGGTCGGATCCGACACCCACCGACC				
					TCTTTGTC
1. IL-1ra β	570	580	590	600	
[882]	TTTGAATTAAATATAAATGACTGAACTCAGCCTA-GAGGTGGCAGCTTGG> 				
IL-1ra-L	TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG				

		810	820	830	840	850
IL-1ra-L		TTCCAGGATAGAGAATCAAGCTGTCAGAGTCATCTTAACAGATCATTATG AAGGTCCTATCTCTTAGTTCGACAGTCTCAGTAGAATTGTCTAGTAATAC				
		C		TAC		T
1. IL-1ra β	620	630	640		660	670
[882]	TTAAAGTTTTGGTTCCCAATGTGTTTTTCGTCATTTTCTTAGGTCATTTTC> 					
IL-1ra-L	TTCCAGGATAGAGAATCAAGCTGTCAGAGTCATCTTAACAGATCATTATG					
		860	870	880	890	900
IL-1ra-L	CGACTGAGTTCACTAGCAGTTCAGCCCATCCATAGCTTACCTCATTCTTA GCTGACTCAAGTGATCGTCAAGTCGGGTAGGTATCGAATGGAGTAAGAAT					
			G			
1. IL-1ra β	680		700	710	720	
[882]	ACGCTG-GTGCTGAGACAGGGCAAGGC-TGCTGTTATCATCTCATT-TTA> 					
IL-1ra-L	CGACTGAGTTCACTAGCAGTTCAGCCCATCCATAGCTTACCTCATTCTTA					
		910	920	930	940	950
IL-1ra-L	CTATCCAAAAGCCACCTCCTCCTCCAAACATCCATTTCTGTACCAAGACC GATAGGTTTTTCGGTGGAGGAGGAGGTTTGTAGGTAAAGACATGGTTCTGG					
		730	740	750	760	
1. IL-1ra β	TAATGAAGAAG-AAGCAATTACTTC--ATAGCAACTGAAG-AACAGGATG> 					
[882]						
IL-1ra-L	CTATCCAAAAGCCACCTCCTCCTCCAAACATCCATTTCTGTACCAAGACC					
		960	970	980	990	1000
IL-1ra-L	CTCACTCGAATGTCACTATCCCAAGATGAAACCTAAAAATCACTTTCCAT GAGTGAGCTTACAGTGATAGGGTTCTACTTTGGATTTTGTAGTGAAAGGTA					
		770	780	790	800	810
1. IL-1ra β	TGGCCTCAGAAG-CAGGAGAGCTGGGTGGTA--TAAGGCTGTCTCTCAA> 					
[882]						
IL-1ra-L	CTCACTCGAATGTCACTATCCCAAGATGAAACCTAAAAATCACTTTCCAT					
		1010	1020	1030	1040	1050
IL-1ra-L	TCTTTCTTGATCTTACCCACCATCCACTCAGCTGCCATGCCAGTTTAG AGAAAGAACTAGAATGGGGTGGTAGGTGAGTCGACGGTACGGGTCAAATC					
		G				
1. IL-1ra β	820	830	840	850	860	
[882]	GCTGTGCTG-T-GTAGGCCACAAGGCA-TCTGCATGAGTGACTTTAAGAC> 					
IL-1ra-L	TCTTTCTTGATCTTACCCACCATCCACTCAGCTGCCATGCCAGTTTAG					

		1060	1070	1080	1090	1100
IL-1ra-L		TTAACCCCCCAAATGCTGCTTCATGCAACCTTCCATTCCCTATTCTTTTG				
		AATTGGGGGGTTTACGACGAAGTACGTTGGAAGGTAAGGATAAGGAAAAC				
			GA			
1. IL-1ra β		870	880	890	900	910
[882]		TCAA-AGACCAAACACTGCTTTCTTCTAGGGGTGGGTATGAAGATGCTTC>				
IL-1ra-L		TTAACCCCCCAAATGCTGCTTCATGCAACCTTCCATTCCCTATTCTTTTG				
		1110	1120	1130	1140	1150
IL-1ra-L		CCAACCCATGATGTAGAGATGTGGATTCATGACATTTTGTTCATACAAC				
		GGTTGGGTACTACATCTCTACACCTAAGTACTGTAAAACAAGTATGTTGA				
		GCGC	C			
1. IL-1ra β		920	930	940	950	960
[882]		AGAGCTCATGTTACCCAGATG-GCATGACTAGCACAGAGCTGAT-C-TCT>				
IL-1ra-L		CCAACCCATGATGTAGAGATGTGGATTCATGACATTTTGTTCATACAAC				
		1160	1170	1180	1190	1200
IL-1ra-L		TCTTCAATAAAACATTATAATATGTGCCCCAAAGATAAAGCTGAAGAATG				
		AGAAGTTATTTGTAAATATTATACACGGGGTTTCTATTTCGACTTCTTAC				
1. IL-1ra β		970	980	990	1000	1010
[882]		GTTTCTGTTTGC-TT-TATTCCTCTTGGGATGATATCATCCAGTCTTT>				
IL-1ra-L		TCTTCAATAAAACATTATAATATGTGCCCCAAAGATAAAGCTGAAGAATG				
		1210	1220	1230	1240	
IL-1ra-L		AGATGAATGTGAAATTAAAGGTTTGCATGTCTTCCTAATCCTAA				
		TCTACTTACACTTTAATTTCCAAACGTACAGAAGGATTAGGATT				
1. IL-1ra β		1020	1030	1040	1050	
[882]		ATATG-TTGCCAATATACCTCATTGTGTGTAAT-AGAA-CCT>				
IL-1ra-L		AGATGAATGTGAAATTAAAGGTTTGCATGTCTTCCTAATCCT				

EXHIBIT E

IL-1ra-L 10 20 30 40 50
GTGTTGCTCCACTGTCAGTCCTCCAGAGCCTCAAGAGATCTTTGGGCCAT
CACAACGAGGTGACAGTCAGGAGGTCTCGGAGTTCTCTAGAAACCCGGTA

IL-1ra-L 60 70 80 90 100
ATCAGCTTTCTTTCCAAAATGAACACACCCAGGGGCAGGAAAGAATGCTC
TAGTCGAAAGAAAGGTTTTACTTGTGTGGGTCCCCGTCTTTCTTACGAG

IL-1ra-L 110 120 130 140 150
TTTCCTTGGTCATTAAGGGGCCTGGGAGTCCTGGACCAGCTTTTCATGCA
AAAGGAACCAGTAATTCCCCGACCCTCAGGACCTGGTCGAAAAGTACGT

IL-1ra-L 160 170 180 190 200
GCTAGACCACTTACATGCAACTAGAGCCTTGACTTTGAAACGAGGGACAA
CGATCTGGTGAATGTACGTTGATCTCGGAACTGAACTTTGCTCCCTGTT

IL-1ra-L 210 220 230 240 250
AAGCATCTCTTGCTAAAGGTAACCTCTGCTGCTTAGAACCCAGCCTCCTC
TTCGTAGAGAACGATTTCCATTGAAGACGACGAATCTTGGGTCGGAGGAG

1. IL-1ra 40
[538] CAGAGGCCTC>
||| ||||
IL-1ra-L CAGCCTCCTC

IL-1ra-L 260 270 280 290 300
ACCACCATCTGATCTATCTTGTTCTCTTCACAAAAGGCTCTGAAGACATC
TGGTGGTAGACTAGATAGAACAAGAGAAGTGTTCGAGACTTCTGTAG

1. IL-1ra 50 60 70 80 90
[538] CGCAGTCACCTA-ATCAC-TCTCCTCCTCTTCCTGTTCCATTGAGAGACG>
|| | | | | | | | | | | | | | |
IL-1ra-L ACCACCATCTGATCTATCTTGTTCTCTTCACAAAAGGCTCTGAAGACATC

IL-1ra-L 310 320 330 340 350
ATGAACCCACAACGGGAGGCAGCACCCAAATCCTATGCTATTTCGTGATTC
TACTTGGGTGTTGCCCTCCGTCGTGGGTTTAGGATACGATAAGCACTAAG

1. IL-1ra 100 110 120 130
[538] ATCTGCCCAC--CCTCTGGGAG-A---AAATCC-A-GCAAGATGCAAGCC>
|| |||| | || | |||| | | | | | |
IL-1ra-L ATGAACCCACAACGGGAGGCAGCACCCAAATCCTATGCTATTTCGTGATTC

	360	370	380	390	400
IL-1ra-L	TCGACAGATGGTGTGGGTCCTGAGTGGAAATTCTTTAATAGCAGCTCCTC				
	AGCTGTCTACCCACACCCAGGACTCACCTTTAAGAAATTATCGTCGAGGAG				
					A
1. IL-1ra	140	150	160	170	
[538]	TTCAGAATCTGGGATGTTAACCAGAAGACCTTCTATCTGAGGAACACCAA>				
IL-1ra-L	TCGACAGATGGTGTGGGTCCTGAGTGGAAATTCTTTAATAGCAGCTCCTC				
	410	420	430	440	450
IL-1ra-L	TTAGCCGCAGCATTAAGCCTGTCACTCTTCATTTAATAGCCTGTAGAGAC				
	AATCGGCGTCGTAATTCGGACAGTGAGAAGTAAATTATCGGACATCTCTG				
1. IL-1ra	190	200	210	220	
[538]	CTAGTTGCTGGA-TA--CTTG-CAAGGACCAAAT-GT-CAATTTAGAAGA>				
IL-1ra-L	TTAGCCGCAGCATTAAGCCTGTCACTCTTCATTTAATAGCCTGTAGAGAC				
	460	470	480	490	500
IL-1ra-L	ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTACCTGGGAATCAA				
	TGTCTTAAGTCACTGTTCTTTTCCCATTTATACCAAATGGACCCCTTAGTT				
			T		
1. IL-1ra	0	240	260	270	280
[538]	AAAGATAGATGTGGTACCCATGAGCCTCATGCTCTGTTCTTGGGAATCCA>				
IL-1ra-L	ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTACCTGGGAATCAA				
	510	520	530	540	550
IL-1ra-L	GGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCCTACTT				
	CCCTTTTCTAGAGACAGAGAAGACACGTCTTTAAGTCCCGTTCGGATGAA				
1. IL-1ra	290	300	310	320	330
[538]	TGGAGGGAAGATGTGCCTGTCTGTGTCAAGTCTGGTGATGAGACCAGAC>				
IL-1ra-L	GGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCCTACTT				
	560	570	580	590	600
IL-1ra-L	TGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCA				
	ACGTCGAATTCCTTTTTTTTATAGTACCTGGACATACACCTCTTCTTCGT				
					G
1. IL-1ra	340	350	360	370	
[538]	TCCAGCTGGAGGCAGTTAACATCACTGACCTG-AGCGAGAACAGAAAGCA>				
IL-1ra-L	TGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCA				

	610	620	630	640	650
IL-1ra-L	CAGAAGCCCTTTCTCTTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTT				
	GTCTTCGGGAAAGAGAAAAAGGTGTTATTTCTTCCGAGGTGAAGACAGAA				
			T		
1. IL-1ra	390	400	410	420	430
[538]	GACAAGCGCTTCGCCTTCATCCGCCAGACAG-TGGCCCCACCACCAGTTT>				
IL-1ra-L	CAGAAGCCCTTTCTCTTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTT				
	660	670	680	690	700
IL-1ra-L	TCAGTCAGTCTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAG				
	AGTCAGTCAGAGAATGGGACCGACCAAGTATCGGTGGAGGTGGTGTAGTC				
1. IL-1ra	440	450	460	470	480
[538]	TGAGTCTGCCGCTGCCCGGTTGGTTCCTCTGCACAGCGATGGAAGCTG>				
IL-1ra-L	TCAGTCAGTCTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAG				
	710	720	730	740	750
IL-1ra-L	GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC				
	CTGTCGGGTAGAAAGAGTGGTTTCCTCTCTCCGTATTGATTATTGTGATTG				
			TATGCC		
1. IL-1ra	490	500	510	520	530
[538]	ACCAGCCCGTCAGCCTCACCAATGACGAAGGCGTCA-TGGT--CACCAAA>				
IL-1ra-L	GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC				
	760	770	780	790	800
IL-1ra-L	TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG				
	AAGATGAATCTAAGACACCTTATTTAGGTCCGATCCGACACCCACCGACC				
1. IL-1ra	540	550	560	570	580
[538]	TTCTACTTCCAGGAGGACGAGT-AGTACTGCCCAGGC-CT-GCTGTTCCA>				
IL-1ra-L	TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG				
	810	820	830	840	850
IL-1ra-L	TTCCAGGATAGAGAATCAAGCTGTCAGAGTCATCTTAACAGATCATTATG				
	AAGGTCCTATCTCTTAGTTCGACAGTCTCAGTAGAATTGTCTAGTAATAC				
1. IL-1ra	590				
[538]	TTCTTGCAAT-GGCAA>				
IL-1ra-L	TTCCAGGATAGAGAA				
	860	870	880	890	900
IL-1ra-L	CGACTGAGTTCACCTAGCAGTTCAGCCCATCCATAGCTTACCTCATTCCTTA				
	GCTGACTCAAGTGATCGTCAAGTCGGGTAGGTATCGAATGGAGTAAGAAT				

	910	920	930	940	950
IL-1ra-L	CTATCCAAAAGCCACCTCCTCCTCCAAACATCCATTTCTGTACCAAGACC				
	GATAGGTTTTTCGGTGGAGGAGGAGGTTTGTAGGTAAAGACATGGTTCTGG				
	960	970	980	990	1000
IL-1ra-L	CTCACTCGAATGTCACTATCCCAAGATGAAACCTAAAAATCACTTTCCAT				
	GAGTGAGCTTACAGTGATAGGGTTCTACTTTGGATTTTTAGTGAAAGGTA				
	1010	1020	1030	1040	1050
IL-1ra-L	TCTTTCTTGATCTTACCCCACCATCCACTCAGCTGCCATGCCAGTTTAG				
	AGAAAGAACTAGAATGGGGTGGTAGGTGAGTCGACGGTACGGGTCAAATC				
	1060	1070	1080	1090	1100
IL-1ra-L	TTAACCCCCCAAATGCTGCTTCATGCAACCTTCCATTCTATTCTTTTG				
	AATTGGGGGGTTTACGACGAAGTACGTTGGAAGGTAAGGATAAGGAAAAC				
	1110	1120	1130	1140	1150
IL-1ra-L	CCAACCCATGATGTAGAGATGTGGATTCATGACATTTTGTTTCATACAAC				
	GGTTGGGTACTACATCTCTACACCTAAGTACTGTAAAACAAGTATGTTGA				
	1160	1170	1180	1190	1200
IL-1ra-L	TCTTCAATAAAACATTATAATATGTGCCCCAAAGATAAAGCTGAAGAATG				
	AGAAGTTATTTTGTAATATTATACACGGGGTTTCTATTTGCGACTTCTTAC				
	1210	1220	1230	1240	
IL-1ra-L	AGATGAATGTGAAATTAAAGGTTTGCATGTCTTCCTAATCCTAA				
	TCTACTTACACTTTAATTTCCAAACGTACAGAAGGATTAGGATT				

AMENDMENTS TO THE SPECIFICATION

Marked Up Version of Replacement Paragraphs of Specification

under 37 C.F.R. 1.121(b)(1)(iii)

Please amend the title at page 1, lines 1-2 to read as follows:

**NUCLEIC ACIDS ENCODING INTERLEUKIN-1 RECEPTOR ANTAGONIST-LIKE
MOLECULES PROTEINS AND USES THEREOF**

AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

- (a) ~~the nucleotide sequence~~ as set forth in SEQ ID NO: 1;
- (b) ~~the nucleotide sequence~~ of the DNA insert in ATCC Deposit No. PTA-1215;
- (c) ~~a nucleotide sequence~~ encoding ~~the~~ a polypeptide as set forth in SEQ ID NO: 2;
- (d) ~~a nucleotide sequence which that~~ hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of any of (a) - (c); ~~and or~~
- (e) ~~a nucleotide sequence~~ complementary to the nucleotide sequence of any of (a) - (e)(d).

2. (Amended) An isolated nucleic acid molecule comprising ~~a nucleotide sequence~~ selected from the group consisting of:

(a) ~~a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in SEQ ID NO: 2, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2;~~

(b) ~~a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 1, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1215, or (a);~~

(e)(a) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, (a), ~~or (b)~~ encoding a polypeptide fragment of at least about 25 amino acid residues, ~~wherein the polypeptide fragment has an activity of the encoded polypeptide as set forth in SEQ ID NO: 2, or is antigenic;~~

(d)(b) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, ~~or any of (a) - (c)~~ comprising a fragment of at least about 16 nucleotides;

(e)(c) a nucleotide sequence ~~which that~~ hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of either ~~any of (a) - (d) or (b);~~ and or

~~(f)(d)~~ a nucleotide sequence complementary to the nucleotide sequence of any of (a) -
~~(d)(c)~~.

3. (Amended) An isolated nucleic acid molecule comprising ~~a nucleotide sequence~~
~~selected from the group consisting of:~~

(a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at
least one conservative amino acid substitution, wherein the encoded polypeptide ~~has an activity of~~
is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2;

~~(b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at~~
~~least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide~~
~~set forth in SEQ ID NO: 2;~~

~~(c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at~~
~~least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide~~
~~set forth in SEQ ID NO: 2;~~

~~(d)(b)~~ a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 ~~which~~
~~having~~ a C- and/or N- terminal truncation, wherein the encoded polypeptide ~~has an activity of the~~
polypeptide set forth in SEQ ID NO: 2 comprises at least 25 amino acid residues;

~~(e)(c)~~ a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at
least one modification ~~selected from the group consisting of that is a conservative amino acid~~
substitutions, ~~amino acid insertions, amino acid deletions, C-terminal truncation, and or N-~~
terminal truncation, wherein the encoded polypeptide ~~has an activity of~~ is at least 70 percent
identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 25 amino acid
residues;

~~(f) a nucleotide sequence of any of (a) - (e) comprising a fragment of at least about 16~~
~~nucleotides;~~

~~(g)(d)~~ a nucleotide sequence ~~which~~ that hybridizes under at least moderately or highly
stringent conditions to the complement of the nucleotide sequence of any of (a) - (f)(c); and or

~~(h)(e)~~ a nucleotide sequence complementary to the nucleotide sequence of any of (a) -
~~(e)(d)~~.

10. (Amended) The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than ~~the promoter DNA for the native IL-1ra-L polypeptide~~ promoter DNA operatively linked to ~~the DNA~~ a nucleic acid molecule encoding ~~the~~ an IL-1ra-L polypeptide.

11. (Amended) The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program ~~selected from the group consisting of~~ that is GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, ~~and~~ or the Smith-Waterman algorithm.

45. (Amended) A nucleic acid molecule encoding a fusion polypeptide comprising the ~~polypeptide~~ nucleic acid molecule of any of Claims ~~13, 14, or 15~~ 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence.

46. (Amended) The ~~fusion polypeptide~~ nucleic acid molecule of Claim 45, wherein the DNA encoding the heterologous amino acid sequence ~~is~~ encodes an IgG constant domain or biologically active fragment thereof.

PENDING CLAIMS

Clean Versions of Pending Claims under 37 C.F.R. 1.121(c)(3)

1. An isolated nucleic acid molecule comprising a nucleotide sequence:
 - (a) as set forth in SEQ ID NO: 1;
 - (b) of the DNA insert in ATCC Deposit No. PTA-1215;
 - (c) encoding a polypeptide as set forth in SEQ ID NO: 2;
 - (d) that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of (a) - (c); or
 - (e) complementary to the nucleotide sequence of any of (a) - (d).

2. An isolated nucleic acid molecule comprising:
 - (a) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, encoding a polypeptide fragment of at least 25 amino acid residues;
 - (b) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, comprising a fragment of at least 16 nucleotides;
 - (c) a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of either (a) or (b); or
 - (d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (c).

3. An isolated nucleic acid molecule comprising:
 - (a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2;
 - (b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 25 amino acid residues;
 - (c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-

terminal truncation, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 25 amino acid residues;

- (d) a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of (a) - (c); or
- (e) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (d).

- 4. A vector comprising the nucleic acid molecule of any of Claims 1, 2, or 3.
- 5. A host cell comprising the vector of Claim 4.
- 6. The host cell of Claim 5 that is a eukaryotic cell.
- 7. The host cell of Claim 5 that is a prokaryotic cell.
- 8. A process of producing an IL-1ra-L polypeptide comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.
- 10. The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than native IL-1ra-L promoter DNA operatively linked to a nucleic acid molecule encoding an IL-1ra-L polypeptide.
- 11. The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program that is GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, or the Smith-Waterman algorithm.
- 42. A composition comprising a nucleic acid molecule of any of Claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.

43. The composition of Claim 42, wherein said nucleic acid molecule is contained in a viral vector.

44. A viral vector comprising a nucleic acid molecule of any of Claims 1, 2, or 3.

45. A nucleic acid molecule encoding a fusion polypeptide comprising the nucleic acid molecule of any of Claims 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence.

46. The nucleic acid molecule of Claim 45, wherein the DNA encoding the heterologous amino acid sequence encodes an IgG constant domain or biologically active fragment thereof.